

**Remarks/Arguments:**

Claims 1-31 are pending. Claims 4, 8-13, 15, 17, 21 and 23-30 are withdrawn from examination. Applicants thank the Examiner for withdrawing the 35 U.S.C. § 112 rejection of claim 1. The Examiner noted that Applicants' argument is persuasive insofar as the claimed method corresponds to the method taught in the specification sentence bridging pp. 12-13. Applicants point out that, while claim 1 includes that method within its scope, the claim is not limited to that specific embodiment. Applicants thank the Examiner for rejoining claim 18 as requested. Claim 23 is amended to correct a grammatical error.

As a preliminary matter, and to avoid confusion as to the identity of various structures identified by number in the application, Applicants invite the Examiner's attention to their response dated March 8, 2007, amending the specification and Figures to correct error in the numbering.

**35 U.S.C. § 103**

All of the claims under examination are rejected under § 103, relying upon Melancon (US 4,922,113) as a secondary reference. But Melancon is not analogous art in relation to the present invention, and therefore does not qualify as prior art against it. The reasons for this conclusion follow.

There are two bases for holding prior art analogous for an obviousness determination: 1) art from same field of endeavor regardless of problem addressed, or 2) art from different fields addressing the same problem. *State Contracting & Engineering Corp. v. Condotte America, Inc.*, 68 USPQ2d 1481 (Fed. Cir. 2003) (reversing district court's holding of non-obviousness and remanding because record presents a factual question as to whether the reference is analogous art); *Wang Laboratories, Inc. v. Toshiba Corp.*, 26 USPQ2d 1767 (Fed. Cir. 1993). Melancon meets neither of these criteria.

The present invention relates to the field of quantitatively measuring binding capacity of a surface containing reactive moieties.<sup>1</sup> The term "binding capacity" refers to the number of reactive moieties per unit area of the surface,<sup>2</sup> and relates to the number of biomolecules capable of binding to the surface via the reactive moieties.<sup>3</sup> The method of the invention can be useful in a medical field, for example, for predicting and quantifying biologically active

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<sup>1</sup> Application, page 2, lines 8-9

<sup>2</sup> Id., page 7, lines 19-20

<sup>3</sup> Id., page 6, lines 23-24

molecules to be bound or bound by reactive moieties of the surface.<sup>4</sup> The term "biologically active molecules" refers to, for example, proteins, cells, antibodies, and/or enzymes.<sup>5</sup> Thus, the problem addressed by the invention is how to quantify the number of reactive sites on a surface capable of binding biomolecules.

Melancon describes methods that are not in the same field as the present invention and that do not solve the same problem as the present invention. Melancon pertains to the field of surface coatings, such as those used to enhance appearance, provide scratch and abrasion resistance, moisture proofing, or adhesion or release characteristics.<sup>6</sup> The problem addressed is how to detect thickness, uniformity, and defects in coatings and detecting marking in coatings that have been applied to substrates.<sup>7</sup> Generally, such coatings can be from about 0.01 to about 200 or more micrometers in thickness, and for release coatings 0.01 to 10 micrometers may be preferred. Examples of such functional coating compositions include primer coatings for enhancing the adhesion of subsequently applied top coatings; protective coatings such as moisture resistant and abrasion-resistant coatings; radiation-sensitive imageable layers; adhesive coatings such as those based on synthetic and natural rubber, acrylic, epoxy, and silicone compounds; and release or abherent [sic; adherent] coatings such as those based on polymers of long chain aliphatic compounds, silicone resins and fluorochemicals.<sup>8</sup>

These facts make clear that Melancon is neither directed to the same field as the claimed invention nor solves the same problems with which the claimed invention is concerned. Consequently, Melancon is not analogous art to this invention and cannot be used in an obviousness rejection against it. Since all of the rejections under 35 U.S.C. § 103 rely upon Melancon as a secondary reference, and because Melancon is not admissible as prior art, all of the rejections should be withdrawn.

Separately, neither Pope & Knigge nor Melancon teaches exposing to exciting radiation a fluorescent moiety that had been attached to a surface and that had subsequently been liberated from it, using a signal from that moiety to calculate a binding capacity as recited in the claims. As a point of clarification, Applicants do not assert that Pope & Knigge does not disclose a "liberated" fluorescent moiety, as stated in the Office Action.<sup>9</sup> Applicants do not

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<sup>4</sup> Id., page 7, lines 16-18

<sup>5</sup> Id., page 7, lines 21-22

<sup>6</sup> Melancon, column 1, lines 20-23

<sup>7</sup> Id., column 1, lines 10-13

<sup>8</sup> Id., column 2, line 60 to column 3, line 4

<sup>9</sup> Office Action, page 9, at point 2.

contest the Examiner's point that the second reaction of Pope & Knigge Figure 6 shows liberation of -S-R' from the surface.<sup>10</sup> Rather, Applicants point out that Pope & Knigge do not contemplate irradiating the liberated moiety and using the signal from that to calculate a binding capacity (or any other parameter). Applicants also assert that Melancon uses only bound (not liberated) moieties for his calculations. Neither reference teaches exposing a liberated fluorescent moiety to radiation. Thus, this feature has not been provided by the cited art. Nor does either reference teach measuring an emitted signal from the liberated moiety. Thus this feature, too, is not provided by the cited art. But it has long been established that, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.<sup>11</sup> Since not all of the claim features are taught or suggested, the rejection should be withdrawn.

Applicants respectfully submit that the foregoing explanations are sufficient to overcome all of the rejections under 35 U.S.C. § 103. Nonetheless, Applicants further traverse the rejections for the following independent and additional reasons, which assume for the sake of argument that the citation of Melancon as prior art had been proper (which Applicants deny).

Claims 1-3, 5-7, 14, 16, 19-20 and 31 are rejected under 35 U.S.C. § 103(a) as unpatentable over Pope and Knigge (US 5,399,501) in view of Melancon (US 4,922,113). Pope & Knigge's invention relates to methods and reagents for the covalent attachment of specific binding members to a solid support.<sup>12</sup> "The general methodology of the present invention involves the modification of a solid phase by the introduction of thiol groups. A specific binding member, e.g., a protein antigen, is also modified to contain thiol-reactive functional moieties such as maleimides or active halogens. The derivatized specific binding member is then added to the thiolated solid phase and reacted to produce a covalent linkage."<sup>13</sup>

The rejection states that it would have been obvious ... to monitor Pope & Knigge's method using fluorescence because Melancon reiterates that, in addition to correlating fluorescence to binding capacity (i.e., "coating weights or thickness"), fluorescence measurements also allow detection of coat uniformity and defects.<sup>14</sup> But the steps performed by Pope & Knigge (as recounted in the Office Action<sup>15</sup>) do not result in a coating, but rather the

<sup>10</sup> Id., page 10, last sentence

<sup>11</sup> *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

<sup>12</sup> Pope & Knigge, Field of Invention

<sup>13</sup> Id., column 8, lines 50-57

<sup>14</sup> Office Action, page 4, second paragraph from last

<sup>15</sup> Id., pages 6-7 at points 1-3

introduction of covalently bound thiol groups onto the surface of the substrate (solid phase). This is a modification of the chemical groups on the surface of the solid phase (for example, alumina<sup>16</sup>). See the final product shown in Pope & Knigge at Figure 6. Figure 6 does not show a coating. Thus, Pope & Knigge teach no coating whose weight or thickness is in need of monitoring, and the purported rationale for applying Melancon's methods is in error.

The rejection also asserts an advantage in detecting "defects," but does not indicate what the Examiner means by that term in the context of Pope & Knigge's invention. Applicants point out that it is not apparent from Pope & Knigge's disclosure that there is in fact a possibility of surface defects, nor is it apparent what kind of "defects" might even be possible, nor is there an indication that such defects (if they existed at all) would even be relevant to Pope & Knigge's objectives. In any case, such defects would not be coating defects, the only type of defect that Melancon teaches his methods to be relevant to, and therefore there would have been no reason to apply those methods to Pope & Knigge's invention.

The courts have held that "...a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known."<sup>17</sup>

The rejection fails to correctly identify any aspect of Pope & Knigge's invention that would profitably be addressed by applying Melancon's methods. No reason is provided that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does, and thus, *prima facie* obviousness has not been established.

As a separate comment, and in an effort to clarify the issues under discussion, Applicants note that the rejection seems to equate binding capacity (relevant to the present invention, but not to Pope & Knigge or Melancon) with coating weights or thicknesses. This is a

<sup>16</sup> Pope & Knigge, column 6, line 41

<sup>17</sup> *KSR Int'l Co. v. Teleflex Inc.*, emphasis added.

misunderstanding. Unlike coating weight and thickness, which are properties of a coating (e.g., such as Melancon uses to prevent abrasion, etc.), binding capacity is a property of a surface. These are not the same thing. Coating weight is measured in grams/unit area of the coating layer, and coating thickness is measured in microns. Binding capacity relates to the number of reactive groups/unit area on a surface, measured in nanomoles/cm<sup>2</sup>,<sup>18</sup> and has nothing to do with the thickness or weight of a coating. A surface can have a binding capacity without any coating at all, as seen in the Examples and discussed throughout the present specification. In any case, as detailed in Applicants' response dated March 13, 2008, Pope & Knigge do not address themselves to binding capacity (as distinct from binding assays, their area of concern), so there would have been no reason to monitor binding capacity.

For all of the above reasons, the combination of Melancon with Pope & Knigge is deficient as a basis for *prima facie* obviousness of claim 1 and its dependents, and so Applicants respectfully request withdrawal of the rejection.

Claim 22 is rejected under 35 U.S.C. § 103(a) as unpatentable over Pope & Knigge and Melancon as applied to claims 1, 2 and 20, and further in view of Burns et al., 56 J. Org. Chem. 2648 (1991). Burns is relied upon to disclose the use of tris(2-carboxyethyl)phosphine as a reducing agent. However, Burns does not remedy the aforementioned deficiencies of the combined Pope & Knigge and Melancon references. Accordingly, a *prima facie* case of obviousness has not been presented, and the rejection should be withdrawn.

Claims 1-3, 14, 16, 18-20 and 31 are rejected under 35 U.S.C. § 103(a) as unpatentable over Clarke & Pai (WO 96/07676) in view of Melancon (US 4,922,113). The rejection relies upon Clarke & Pai to disclose binding a fluorescent moiety to a surface, and also to disclose subsequently cleaving a bond or group linking that fluorescent moiety to the surface, both as recited in instant claim 1. The rejection considers that 5,5'-thiobis(2-nitrobenzoic acid) ("DTNB") is a fluorophore,<sup>19</sup> but there is no evidence of record that this is the case. Clarke & Pai do not refer to it as such, nor in fact do they discuss fluorescence at all. Applicants note that, in the present application, DTNB is used to link a fluorescent moiety to a surface, but it is not itself the fluorescent moiety. (Claim 6 recites examples of fluorescent compounds that can be used to provide the fluorescent moiety.) Figure 2 shows in schematic form how the fluorescent moiety (designated "FI") is attached to a surface using DTNB to form a linking

<sup>18</sup> Specification, page 18, lines 8-9

<sup>19</sup> Office Action, page 7 at point 2.

group. See also page 6 at lines 13-18, which describe this process. Thus, the rejection has not provided the claim feature reciting binding a fluorescent moiety to a surface.

The rejection also appears to conclude that the presence of a pink supernatant<sup>20</sup> indicates that a fluorescent moiety has been liberated from the surface as claimed, but Applicants contest this assertion. The presence of a pink color may indicate the presence of a chromophore (i.e., a colored group) in the supernatant, but it does not indicate the presence of a fluorescent moiety. Applicants note that many materials are colored but not fluorescent, and there is no evidence that Clarke & Pai's supernatant contains a fluorescent moiety.

The rejection states that it would have been obvious ... to monitor Clarke & Pai's method using fluorescence because Melancon reiterates that, in addition to correlating fluorescence to binding capacity (i.e., "coating weights or thickness"), fluorescence measurements also allow detection of coat uniformity and defects.<sup>21</sup> Applicants note, however, that there is no indication in Clarke & Pai of any interest in binding capacity, nor do Clarke & Pai employ a coating. Thus, the person of ordinary skill would not have seen a reason to apply Melancon's coating-oriented methods to Clarke & Pai's invention. As noted earlier above, *prima facie* obviousness requires some rationale for making the proposed combination, and in the absence of such the rejection should be withdrawn.

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<sup>20</sup> Id., page 7, point 3.

<sup>21</sup> Id., page 8, lines 5-8

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Conclusion

Applicants submit that the application is now in condition for allowance, and respectfully request reconsideration and notification of same. Applicants invite the examiner to contact their undersigned representative, Frank Tise, if it appears that this may expedite examination.

Respectfully submitted,



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